

2-2-94



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: EPA File Symbol: 499-URG

From: Mark J. Perry, Biologist
Precautionary Review Section
Registration Support Branch
Registration Division (7505W)

MJP
2-2-94

To: Dennis Edwards, PM 19
Insecticide-Rodenticide Branch
Registration Division (H7505C)

Applicant: Whitmire Research Laboratories, Inc.
3568 Tree Court Ind. Blvd.
St. Louis, MO 63122

FORMULATION FROM LABEL:

	<u>% by wt.</u>
<u>Active Ingredient(s):</u> Chlorpyrifos (0,0-Diethyl 0-(3,5,6-Trichloro-2-Pyridyl) Phosphoro- thioate)	0.5
<u>Inert Ingredient(s):</u>	99.5
Total:	100%



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BACKGROUND

Whitmire Research Laboratories, Inc. submitted acute oral, acute dermal, acute inhalation, eye irritation, dermal irritation and dermal sensitization studies in support of Whitmire TC 100. Whitmire TC 100 is a crack and crevice/wood injection insecticide system containing Chlorpyrifos as the active ingredient. All six studies were performed by Biosearch Incorporated and the MRID numbers are 430729-02 through 430729-07.

RECOMMENDATION

The acute oral, acute dermal, acute inhalation, eye irritation and dermal irritation studies are acceptable as core guideline data. The acute inhalation study received a core minimum grade since only two doses were employed. The guidelines state that if a limit test is unsuccessful, a three dose level LD₅₀ study should be performed.

The dermal sensitization study received a core minimum grade since the test material application and occlusion procedure during the challenge phase was not fully described in the report. However, since a positive response (20% or greater positive response in test group over naive control) was demonstrated, it can be concluded that the exposure was adequate.

LABELING

1. The appropriate signal word is "caution."

2. The Precautionary Statements should read as follows:

Harmful if absorbed through skin. Avoid contact with skin, eyes or clothing. Prolonged or frequently repeated skin contact may cause allergic reactions in some individuals. Wash thoroughly with soap and water after handling.

3. The Statements of Practical Treatment should read as follows:

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

4. The statement "contains petroleum distillates" should appear in close proximity to the ingredient statement.

ACUTE TOXICITY PROFILE

Acute Oral.....	Category 4/G
Acute Dermal.....	Category 3/G
Acute Inhalation.....	Category 4/M
Eye Irritation.....	Category 4/G
Dermal Irritation.....	Category 4/G
Dermal Sensitization.....	Pos /M

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1)

Product Manager:32
MRID No.:430729-02
Testing Facility:Biosearch, Inc.
Author(s):D. Gabriel
Species:Rat

Reviewer:M. Perry
Report Date:12/3/93
Report No.:93-7889A

Age:--
Weight:212-299 g
Source:Buckshire Corp.
Test Material:Whitmire TC-100
Quality Assurance (40 CFR §160.12):Present

Conclusion:

1. LD₅₀ (mg/kg): Males= --
 Females= --
 Combined= > 5.0 mg/kg
2. The estimated LD₅₀ is > 5.0 mg/kg
3. Tox. Category:IV Classification:Guideline

Procedure: The fasted test animals were dosed (as indicated below) by gavage. The animals were observed for mortality and signs of toxicity at least daily during the 14 day observation period. Body weights were recorded on the day of dosing and weekly thereafter or at sacrifice.

Results:

Dosage g/kg	(Number Killed/Number Tested)		
	Males	Females	Combined
5.0	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings: No clinical signs of toxicity were observed during the study. No gross abnormalities were noted in the animals terminated at sacrifice.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager:32
MRID No.:430729-03
Testing Laboratory:Biosearch Inc.
Author(s):D. Gabriel
Species:Rabbit

Reviewer:M. Perry
Report Date:12/3/93
Report No.:93-7889A

Weight:2.35-2.87 kg
Source:Davidson's Mill Farm
Test Material:Whitmire TC-100
Quality Assurance (40 CFR §160.12):Present

Summary:

1. LC₅₀ (mg/kg): Males= --
Females= --
Combined= > 2.0 g/kg
2. The estimated LD₅₀ is > 2.0 g/kg
3. Tox. Category:III Classification:Guideline

Procedure: The undiluted test material was applied to the clipped exposure sites (approx. 10% of body surface) of the animals and occluded for a period of 24 hours. The animals were observed for mortality and signs of toxicity at least daily during the 14 day observation period. Body weights were recorded on the day of dosing and weekly thereafter or at sacrifice.

Results:

Reported Mortality

DOSAGE g/kg	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2.0	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings: The only clinical signs observed were dermal irritation. No gross abnormalities were noted in the animals terminated at sacrifice.

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager:32

MRID No.:430729-04

Testing Laboratory:Biosearch, Inc.

Author(s):R. Hershman

Species:Rat

Weight:201-295 g

Source:Buckshire Corp.

Test Material:Whitmire TC-100

Quality Assurance (40 CFR §160.12):Present

Reviewer:M. Perry

Report Date:11/1/93

Report No.:93-7889A

Summary:

1. LC₅₀ (mg/kg): Males= --
Females= --
Combined= > 5.4 mg/L
2. The estimated LC₅₀ is > 5.4 mg/L
3. Mean Concentration: --
4. Tox. Category:IV Classification:Minimum

Procedure: The animals were exposed to the test atmosphere for four hours within a 230 liter chamber. A jet nebulizer and syringe pump were used for atmosphere generation. Chamber concentration was determined gravimetrically and analytically (four times each exposure) and particle size distribution was measured once each hour with a cascade impactor. After a four hour exposure, the animals were observed for mortality and signs of toxicity at least daily during the 14 day observation period. Body weights were recorded on days 0, 7 and 14.

Deviation From §81-3: See recommendations

Results:

Reported Mortality

Exposure Concentration mg/L	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
5.4	1/5	0/5	1/10
5.7	2/5	0/5	2/10

Symptoms & Gross Necropsy Findings: Clinical signs included inactivity, deep respiration and tan-stained muzzles. No gross abnormalities were observed upon necropsy except in one animal which exhibited dark red lungs containing liquid.

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mg/l							Air Flow [l/m]
Nom Conc	Grav Conc	Analyt Conc	MMAD	GSD	Temp[C]	Hum%	
15.6	1.37	5.4	2.92	0.09	21.0	67-75	37
16.0	1.38	5.7	2.91	0.05	21-22	60-61	37

7.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (\$81-4)

Product Manager:32
MRID No.:430729-05
Testing Laboratory:Biosearch Inc.
Author(s):G. Moore
Species:Rabbit
Sex:6 female
Weight:--
Source:Davidson's Mill Farm
Dosage:One second spray from 10 cm
Test Material:Whitmire TC-100
Quality Assurance (40 CFR \$160.12):Present

Reviewer:M. Perry
Report Date:11/30/93
Report No.:93-7889A

Summary:

1. Toxicity Category:IV
2. Classification:Guideline

Procedure: A one second spray of the test material from 10 cm was directed into the right conjunctival sac of each animal and the eyelids were held together for about one second. The test eyes were evaluated at 1, 24, 48, 72 hours and at 4 and 7 days.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	0/6	0/6	0/6	0/6	0/6		
Iris	0/6	0/6	0/6	0/6	0/6	0/6		
Conjunctivae								
Redness	0/6	0/6	0/6	0/6	0/6	0/6		
Chemosis	0/6	0/6	0/6	0/6	0/6	0/6		
Discharge	0/6	0/6	0/6	0/6	0/6	0/6		

Comments: No "positive" results were noted during the ocular observations.

DATA REVIEW FOR SKIN IRRITATION TESTING (\$81-5)

Product Manager:32
MRID No.:430729-06
Testing Laboratory:Biosearch Inc.
Author(s):G. Moore
Species:Rabbit

Reviewer:M. Perry
Report Date:11/30/93
Report No.:93-7889A

Age:--
Sex:--
Weight:--2.43-2.82 kg.
Dosage:0.5 ml
Test Material:Whitmire TC-100
Quality Assurance (40 CFR \$160.12):Present

Summary:

1. The Primary Irritation Index= --
2. Toxicity Category:IV
3. Classification:Guideline

Procedure: A dose of 0.5 ml of test material was applied to the clipped exposure sites (approx. 6 cm²) and occluded for a period of four hours. Dermal evaluations were performed at 30-60 minutes, 24, 48, and 72 hours and at 7 days.

Results: The only irritation noted at or beyond the 72 hour evaluation was very slight erythema in one animal.

DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager:32
MRID No.:430729-07
Testing Laboratory:Biosearch Inc.
Author(s):P. Romanelli
Species:Guinea pig
Weight:337-447 g
Source:Davidson's Mill Farm
Test Material:Whitmire TC-100
Positive Control Material:DNCB
Quality Assurance (40 CFR §160.12):Present

Reviewer:M. Perry
Report Date:12/3/93
Report No.:93-7889A

Method:Buehler

Summary:

1. According to the results of this study, the subject product is a dermal sensitizer.
2. Classification:Minimum

Procedure: The test animals were induced at clipped exposure sites with a 75% concentration (in mineral oil) of the test material three times a week for a total of nine applications. Each application was occluded and contact was maintained for six hours except for the first induction exposure which included a 24 hour contact period. Following a fourteen day rest period, the test group was challenged with a 50% concentration (also in mineral oil) and at a naive site for 24 hours. A group of naive control animals were also employed in the study.

The positive control study was performed with DNCB and demonstrated a positive response.

Deviation From §81-6: See recommendations

Results:

26 Hours

Test group:	grade 0 = 4/10
	grade +/- = 4/10
	grade 1 = 2/10

Naive control group:	grade 0 = 2/5
	grade +/- = 3/5

ACUTE TOX ONE-LINER

1. PC CODE: 059101
2. CURRENT DATE: 2/2/93
3. TEST MATERIAL: Chlorpyrifos 0.5%

Study/Species/Lab/ Study#/Date	MRID No.	Results	Tox. Cat.	Core Grade
81-1, RAT, BIOSEARCH INC., 93-7889A, 12/3/93	430729-02	LD50 > 5.0 G/KG	IV	G
81-2, RABBIT, BIOSEARCH INC., 93- 7889A, 12/3/93	430729-03	LD50 . 2.0 G/KG	III	G
81-3, RAT, BIOSEARCH INC., 93-7889A, 11/1/93	430729-04	LC50 > 5.4 MG/L	IV	M
81-4, RABBIT, BIOSEARCH INC., 93- 7889A, 11/30/93	430729-05	NO "POSITIVE" RESPONSES	IV	G
81-5, RABBIT, BIOSEARCH INC., 93- 7889A, 11/30/93	430729-06	VERY SLIGHT ERYTHEMA AT 72 HRS.	IV	G
81-6, GUINEA PIG, BIOSEARCH INC., 93- 7889A, 12/3/93	430729-07	POSITIVE RESPONSE	---	M

Core Grade Key:

G = Guideline
M = Minimum
S = Supplementary